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# THE MEDICAL JOURNAL OF AUSTRALIA.

VOL. I.—8TH YEAR.

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No. 13.

## DEVELOPMENTS IN THE PRODUCTION OF THERAPEUTIC SERA IN AUSTRALIA.<sup>1</sup>

By W. J. Penfold, M.B., B.Hy.,

From the Commonwealth Serum Laboratories.

### ANTITOXINS.

#### Diphtheria Toxin.

In the production of anti-diphtheritic serum, the first essential is a good diphtheria toxin. We have been able, at the Commonwealth Serum Laboratories, to produce fairly satisfactory toxins, 47% of them being so potent that  $\frac{1}{50}$  of a cubic centimetre has been sufficient to kill 250 gramme guinea-pigs within fifty-six hours.

Compared with the toxins which have been described in the literature, these appear to be rather weak. For example, MacConkey has described toxins killing at  $\frac{1}{300}$  c.cm. and even  $\frac{1}{1400}$  c.cm.. A reference to his paper does not, however, disclose the weights of the pigs, nor the times of death. It is evident, however, that his toxins were definitely stronger than ours. This is partly accounted for by the fact that during the war we were unable to obtain Witte's peptone, whereas MacConkey had access to that peptone during the years that he was making the toxins which he reviewed.

Lewis Davis, from the Laboratories of Parke, Davis & Co., reports that he finds 90% of his toxins useful, that is to say, they have an L+ dose of 0.5 c.cm. or less. We cannot compare our results with his, since we have invariably determined the M.L.D. rather than the L+ dose and the number of M.L.D. in the L+ dose varies in the case of different toxins.

Bunker, an American worker, reports that for one litre of good toxin that can be used, many litres of bad toxin have to be thrown out. His experience seems to have been very definitely worse than ours, since, as previously stated, 47% of our toxins are useful.

It has been reported by Macé that it is possible with Martin's broth to get toxins so strong that 0.01 to 0.002 c.cm. will kill a 250 gramme guinea-pig in from fifteen to forty hours. He does not give us any information about the average toxins obtained with Martin's broth.

We have used various broths here (Martin's broth, broth containing Fairchild's, Parke, Davis's or May & Baker's peptones), but we have had no evidence in favour of any of these other peptones being superior to Martin's for the production of diphtheria toxin.

It is to be regretted that in the standardization of toxins for routine purposes authors have not used a uniform method, so that it is quite impossible to compare all the results.

#### Diphtheria Antitoxin Results.

Lewis Davis has reported that 78% of new horses, on the first bleeding after the first immunization against diphtheria toxin, gave an average of 200 or

more units per cubic centimetre; 36% of this 78% gave less than 500 units, that is to say, 28% of the total, so that 50% of the total number of horses did not give 500 units on their first bleeding.

We have immunized against diphtheria toxin 33 new horses and have had 78% that have given over 400 units per cubic centimetre on the first bleeding, so that the usefulness of our toxin, as judged by the immunity response in the animals, is very definitely greater than that described by Lewis Davis.

Of the horses described by him, 15% gave a unitage of over 1,000 per cubic centimetre. A comparison of our results with that figure is not possible, because we have been accustomed to test our horses on the first immunization for 400 and 600 units, but not, as a rule, for a higher unitage. Our practice is to use the serum having 600 or more units for issue as unconcentrated serum, while that having 400 units and less than 600 units is concentrated.

In the case of one horse the unitage was tested because we had reason to think that it was very high; we found the antitoxin content of the first bleeding to be higher than 1,300 units. Owing to the shortage of animals, no tests were made of higher dilutions of the serum, so that we do not know what its actual antitoxin content was.

We have recently issued diphtheria antitoxin containing 1,600 units per cubic centimetre. It is a remarkably clear product, not disposed to precipitate and of very low protein content.

#### Reaction of Culture Medium.

At this juncture it is advisable for me to digress from the general tenor of my remarks in order to deal with a matter which has recently become of great importance in every department of our work. The matter to which I refer is hydrogen-ion concentration.

In many bacteriological processes it is necessary to know the reaction of the liquids with which we are dealing. Until quite recently this was determined in a rough manner by titration methods, but, owing to the work of Clark and Lubs and others, the estimation of reaction by hydrogen-ion concentration methods has been shown to be imperative in bacteriological work.

We have found that a good tuberculin can be made by growing the tubercle bacillus on a glycerine veal broth with a hydrogen-ion concentration of 7.2. American workers have shown that the maximum growth of the pneumococcus is obtained in broth with a hydrogen-ion concentration of 7.8. A good diphtheria toxin can frequently be obtained in a broth having a hydrogen-ion concentration of about 8, while serum for concentration requires a reaction of about 8.3.

Two broths which were found to give similar reactions under the old system, may be found to give entirely different hydrogen-ion concentrations.

Since hydrogen-ion concentration is the essential factor in reaction, the old method of titration has for practical purposes been almost entirely abandoned.

<sup>1</sup> Read at a Meeting of the New South Wales Branch of the British Medical Association on November 26, 1920.

Hydrogen-ion estimations may be made by electro-metric methods or by means of a series of indicators. The colours produced by certain hydrogen-ion concentrations in solutions of indicators have been ascertained by various workers and all have agreed that for bacteriological purposes phenol red is the most generally useful indicator to employ. It indicates hydrogen-ion concentrations from 6.9 to 8.1; since the hydrogen-ion concentration of the blood is 7.5, it is at once evident that this indicator gives us information of reaction over that range in which we, as bacteriologists, are interested. This indicator is used most easily in bacteriology, according to the Barnett-Chapman (1918) method. The scale consists in a series of tubes in one row containing  $\frac{1}{200}$  hydrochloric acid and a second series of tubes in a parallel row containing  $\frac{1}{20}$  alkali; ten drops of dye are distributed in a certain definite manner between each pair of tubes in such a way as to get, on looking through the double tubes, a yellow colour at one end of the scale, a red colour at the other end of the scale and a series of intermediate colours between.

In order to use the scale so produced for hydrogen-ion concentration work, a certain definite quantity (2 c.c.m.) of the broth to be titrated is taken and to this is added four times the volume of water, then the same amount of dye (phenol red) as is contained in each pair of tubes, i.e., ten drops. The colour produced is then compared with the colours of the scale; such a comparison gives the hydrogen-ion concentration of the broth being titrated.

This method depends upon the fact that if a solution be diluted, its hydrogen-ion concentration is not materially altered.

We have adopted this method throughout almost the whole of the work of the Institute.

Until quite recently in making our diphtheria toxin the reaction was adjusted by titration with litmus, the broth being made —7 to litmus. Since phenol red has been adopted for titration, the reaction has doubtless been more correct, but in spite of that fact the toxin produced is not by any means uniformly potent.

#### *Bleeding.*

The method that we have adopted here in bleeding our animals to obtain serum is to receive the blood into 25 c.c.m. of potassium oxalate solution in two-litre, wide necked Winchester quarts. These Winchester quarts are then placed in the hot room (37° C.) and during the course of two or three hours sedimentation of the red cells occurs. The supernatant plasma is then removed and the red cells are returned to the horses according to the method previously described in this *Journal*.<sup>1</sup> This method has now been universally adopted in all our bleedings and up to the present no untoward results have occurred to shake our confidence in it. With this new method we have been able to increase the yields from our animals by more than 100%.

It has been objected to the method that the oxalate must be more or less toxic for the horses and that a considerable quantity of it must be returned with the red cell fraction. We have not been able to find any evidence of intoxication resulting from its use. The horses are in splendid condition and compare very

favourably with those of any of the serum institutes that I have visited.

A leading American house is at the present time giving the method a trial, only instead of using oxalate they are using citrate. Citrate is believed to be less toxic than oxalate, but it is by no means free from toxicity and the volume of the solution of citrate necessary to prevent clotting of the blood is greater than the volume of the corresponding oxalate solution; consequently the dilution of the plasma is greater. It appears, therefore, desirable to use oxalate in preference to citrate. It is, however, only a matter of detail.

#### *Serum Concentration.*

In recent years great progress has been made in the direction of concentrating serum, e.g., in the case of anti-diphtheritic and anti-tetanic sera a seven- to a nine-fold concentration is practicable, so that though a plasma direct from the horse may contain only 300 units per cubic centimetre, it is feasible to raise the unitage, by concentration, to 2,100 units per cubic centimetre or even more. At the same time, the fibrinogen, eu-globulin and serum albumin are eliminated, so that the amount of horse protein per unit of antitoxin is very greatly diminished. The serum so concentrated is less liable than ordinary serum to produce serum disease, very largely on account of its small protein content per unit of antitoxin and probably also because the protein is to some extent altered during the concentration process.

We have been using ammonium sulphate for this process, as recommended by Gibson, Banzhaf, Homer and Heinemann, all of whom have contributed to the development of the technique of the subject.

The greatest difficulty that we have experienced in the concentration work has been the filtration of the final product through Pasteur Chamberland "F" candles. It was quite common in the early days to find that we could not get more than about a couple of litres of concentrated serum through half a dozen of such candles; not only did the candles block, but the ultra-filter formed during the process occasioned heavy losses of antitoxin. Amongst the causes contributing to this difficulty may be mentioned the fact that the plasma was concentrated almost immediately after it was drawn from the horse and that it was filtered soon after being concentrated. We have now, however, got large stocks of serum accumulating and it is never necessary for us to attempt the filtration of recently concentrated diphtheria antitoxin. The result is that at the present time we are able to filter concentrated serum through Pasteur Chamberland "F" candles without serious difficulty and without any considerable loss of antitoxin.

Difficulty in the filtration of the end product may also arise from the precipitation of the serum protein from the metal of the filter cases. This has only to be recognized in order to be avoided.

But few complaints have been made of serum disease following the use of our concentrated diphtheria antitoxin; I believe that with our accumulating stocks of antitoxin such ageing of the product will be possible as practically to abolish serum disease.

At this stage I might draw your attention to the work of Gay and Chickering on the biological method

<sup>1</sup> *The Medical Journal of Australia*, September 25, 1920.



of concentration; it has been tried in the case of anti-pneumococcal serum, with the result that a sixty-fold concentration of antibody has been effected—a degree of concentration of an entirely different order from anything that has ever been obtained by the ammonium sulphate method in the case of either anti-diphtheritic or anti-tetanic serum. The product, however, is uncertain and unstable; the Rockefeller workers who experimented with it, preferred to use the unconcentrated serum in cases of pneumonia.

This concentration of anti-pneumococcal serum was effected by the mixing of a solution of pneumococcus with its anti-serum and extracting the precipitate with alkali. A highly protective water-clear solution was obtained.

The ammonium sulphate method of concentration is not available for use with anti-pneumococcal serum, because with that method bacterial contamination is inevitable in some stage of the process and the bacterial products that may arise, render disagreeable the intravenous injection of the serum necessary in such work.

In 1916 no concentration of serum was undertaken at the Pasteur Institute, Paris (personal communication). This is quite unlike the practice in all English-speaking countries, since the concentration of the serum has very definite and evident advantages. In the French method of sterilizing the serum by intermittent heating after it has been placed in ampoules, a considerable fall in antitoxin content occurs. It is not possible to produce a serum of very high potency under these conditions.

#### Tetanus Toxin.

The work of Anderson, of the Hygienic Institute in Washington, showed that it was possible to produce a highly potent tetanus toxin. By using his method Miss Wilcox, of the New York Public Health Laboratories, has been able to get tetanus toxins killing 350 gramme guinea-pigs on the fourth day with quantities of from 0.00004 to 0.000025 c.e.m.. Moreover, the method gave these results regularly.

In 1916, on visiting several laboratories in Europe, I found that tetanus toxins were being used there having an M.L.D. of 0.0005 c.e.m..

We have used Anderson's method, but have not been able, until very recently, to get toxins of the high toxicity of the American authors.

On considering carefully why the European toxins and our toxins were inferior, it occurred to me that the trouble might be due to the difference in the methods used for expressing reaction in culture media in America and in Europe, a +1 in America being equivalent to a +10 of the Eyre scale. Moreover, much of the American work had been done with Witte's peptone, which was not obtainable in Australia during the first year of our work on tetanus toxin production.

We have been fortunate recently in securing some Witte's peptone, and using that at the +10 reaction of English workers we have been able to get a toxin killing at 0.000025 c.e.m..

It is probable that both these factors contributed to the difference between our results and those obtained by the American workers, but it seems more likely that the difference in expressing reaction is the chief explanation rather than the obtaining of

the Witte's peptone. Miss Wilcox has shown definitely that with Martin's and other peptones she has been able to get highly potent toxins, although not quite so regularly as with Witte's.

#### Tetanus Antitoxin.

For the immunization of our horses against tetanus toxin we have used Park's method. It has the great advantage of yielding a reasonably good antitoxin in four months, as against six, eight or even twelve months required by the old methods.

According to Park's method the horse is given initially a dose of tetanus antitoxin; this enables a relatively quick immunization to be carried out. The immunization, however, is by no means straightforward; we have had one horse die of tetanus from the toxin with which it was inoculated and that experience has been paralleled in many laboratories.

In the first instance our horses were bled rather early for tetanus antitoxin, because of an urgent demand for it, but on the re-immunization of the first six of these horses five of them gave an average response of 175 American units per cubic centimetre on the first bleeding. The tetanus antitoxin at present on the local market commonly contains about 170 units per cubic centimetre.

We have concentrated several batches of tetanus antitoxin and we are now having the same trouble with their filtration as we had with the first batches of concentrated diphtheria antitoxin. We fully expect that they will filter better on ageing, as the corresponding batches of diphtheria antitoxin did.

The position is that the Laboratories can at the present moment supply any reasonable quantity of unconcentrated tetanus antitoxin and that within a short time they will have on the market a concentrated tetanus antitoxin very suitable for the treatment of the declared disease.

#### ANTIBACTERIAL SERA.

##### Anti-Pneumococcal Serum.

Eyre's early work showed that serological varieties existed amongst the pneumococci and that erratic results in treatment were due to these serological varieties.

Kindborg even went so far as to believe that there were no types amongst the pneumococci; that they were an entirely heterogeneous group.

Neufeld described four types, one being very common, one fairly common and two individual separate strains. This work has been amplified at the Rockefeller Institute and also by Lister in South Africa.

In 1913 the American workers described four types of pneumococci, the fourth type consisting of a heterogeneous group, but Types I., II. and III. being well-defined separate entities. Subsequently atypical varieties of the second type were described by Avery and Stillman, so that now we have twelve sub-types of atypical Type II..

Lister, in 1913, published his preliminary typing of the South African pneumococci and extended that work a little later, so that he has found no less than ten types amongst the strains that he has examined.

In making an effective anti-pneumococcal serum, cognizance must be taken of all these types, since the immunizing value of the type sera is highly specific. In attempting to make an anti-pneumococcal serum

for use in Australia, it behoved us to examine the Australian pneumococci with a view to ascertaining the prevailing types.

We have examined, up to the present, nearly 100 pneumococcal strains. The first 51 were distributed in the following way:

- 30% Type I.;
- 10% Type II.;
- 20% Type III.;
- 8% Type "Setch"; and
- 32% heterogeneous.

These 51 strains were all isolated from acute respiratory infections, the great bulk of them being lobar pneumonia.

The corresponding American figures are:

- 33% Type I.;
- 29% typical Type II.;
- 4% atypical Type II.;
- 13% Type III.;
- and
- 20% heterogeneous.

On comparing these two series of percentages, the following are the main points of interest:

- Type I. seems to be almost as prevalent here as in America;
- Type II. is very definitely less prevalent;
- Type III. is slightly more prevalent;
- Type "Setch" seems to be a new Australian type;

The heterogeneous group in the Australian series is very definitely larger than in the American series.

An effort is being made at the present time to see if subsidiary types cannot be found in this large heterogeneous group.

Work done elsewhere has shown that Type I. pneumococcal serum is very definitely valuable in the treatment of lobar pneumonia in man, whereas sera against other types, though very effective in animal experiments, appear to be practically useless in clinical practice.

We therefore proceeded to make a Type I. serum. In doing this the method recommended by the Rockefeller workers was pursued, but the result was not found very satisfactory. Five months elapsed before we got a satisfactory agglutination titre against virulent pneumococci; at the end of that time a highly potent serum was obtained, judged either by protective tests in mice or by agglutination tests against virulent pneumococci. Agglutination tests in the case of pneumococcal serum must be done against virulent pneumococci. The avirulent pneumococci agglutinate in very high dilutions of serum—even up to from 1 in 2,000 to 1 in 5,000—whereas the same pneumococci in the virulent state will give quite specific and valuable agglutination reactions at dilutions not higher than 1 in 40 or 1 in 80.

According to the Rockefeller method of immunizing horses, the pneumococci grown in broth cultures and obtained from such cultures by centrifugalization are inoculated into the horse after the pneumococci are killed by heat. Daily injections are given every alternate week.

After two or three weeks' treatment in this way, samples of the serum are tested for potency and agglutinative capacity. If these tests are not satisfactory, the horse is then immunized further with

fairly large doses of living pneumococci and this is continued until the titre is satisfactory.

In our more recent work we have been inclined to continue the immunization throughout with killed pneumococci, a method practised by the French. We have in that way obtained potent serum without the disturbance in the health of the horse that was caused by the use of living pneumococci.

#### *The Use of Pneumococcal Serum in Type I. Pneumonias.*

In using this serum against Type I. pneumonia it is necessary for the practitioner to have the pneumococcus infecting his patient typed; moreover, that typing should be done quickly. For that purpose the best method is to inoculate a little of the sputum of the pneumonic patient into the peritoneal cavity of the mouse, eight hours later to kill the mouse, to wash out the peritoneal cavity with saline solution and to do a precipitin test against the sera specific for the different types. (Blake.)

Another method for typing the pneumococcus is to inoculate glucose rabbit-blood broth with the sputum and to use the supernatant fluid from that culture for precipitin work. (Avery.) A certain error exists in this method; moreover, it is no more rapid than the mouse method. I think, therefore, that it is not quite so good for general use.

Although for some time we have had large quantities of Type I. pneumococcal serum on hand, the demand for it has been singularly small. This is partly due to the fact that the clinical bacteriologists in Australia have not yet taken up very extensively the typing of pneumococci; it may also be partly due to the indifference of the practitioner.

#### *Anti-Meningococcal Serum.*

Our first attempt to make anti-meningococcal serum was carried out according to the method of Amoss. He recommends the injection of the antigen daily for three days and then an interval of rest, after which the antigen is again injected daily for three days. This treatment is continued with increasing doses until  $4\frac{1}{2}$  serum agar slope cultures are given in one dose. When large doses are given, he recommends the injection of a desensitizing dose in the morning of the day on which the large injection is to be made. All injections, according to this method, are given intravenously.

We followed Amoss's instructions very closely in our early immunizations, but did not find that we got a very good response, as judged by the agglutinin content of the serum. We, therefore, discontinued the use of his method and confined our injections to one per week, our final dose rising to twenty agar slopes. By this method we were able to get highly potent agglutinating sera.

It was very striking that the agglutinin responses to Types I. and III. were very much greater and very much earlier than the agglutinin response to Type II.. Moreover, we found that if a horse had been already immunized against Types I., II. and III., on re-immunization it could be effectively immunized with Type II. alone, that is to say, the serum derived from a horse so immunized would have a high agglutinating titre for Gordon's Types I., II. and III..

We have not found Gordon's fourth type in Aus-

tralia and it seems unlikely that it is of serious practical importance in any country.

We have had very satisfactory clinical reports of the use of our anti-meningococcal serum, but apart from an epidemic at Townsville, occurring on a ship and in the quarantine station there, the treatment of meningococcal meningitis by this serum has been confined to cases more or less sporadic in character.

#### Anti-Dysenteric Serum.

The work of Ruffer, Willmore and Savage has shown that anti-dysenteric serum made by the injection of living strains is highly effective in the actual treatment of acute dysentery. Their serum was made from Shiga, Flexner and El Tor strains and was highly polyvalent in character.

Martin, at the International Medical Congress in 1913, stated that anti-dysenteric serum was the second most valuable serum that we had for the treatment of disease.

We have made a special Shiga serum and also a polyvalent anti-dysenteric serum.

In the case of the Shiga serum we started our injections with one twentieth of an agar slope, giving weekly doses up to three quarters of a slope in size. These doses all consisted of living organisms and were given intravenously. The resulting serum was highly protective in rabbits and had a fairly high agglutinating titre.

We have had difficulty with this method of making anti-dysenteric serum, since two of our horses have died from Shiga infections; in each case we were able to isolate Shiga's bacillus either from the discharges or from the body *post mortem*.

We have found that 0.01 c.cm. of this serum would protect a rabbit against 500 million living *B. dysenteriae* (Shiga). One hundred million Shiga bacilli killed control rabbits of similar weights.

#### Anti-Gonococcal Serum.

In the case of anti-gonococcal serum the horses were inoculated with living gonococcal cultures. The initial dose was half a slope, because the horses that were used for the purpose had had a preliminary immunization with meningococci. It has been shown by Arkwright and others that gonococci and meningococci have close serological affinities.

The immunization was continued weekly until doses of twelve slopes could be given intravenously.

The serum obtained from horses so immunized has been tried in the Alfred Hospital in Melbourne, in clinical cases, with very good results.

In immunizing one horse intravenously with the gonococcus, three minutes after the fourth intravenous injection the animal fell down dead. This is the only case of what may have been acute bacterial anaphylaxis that has occurred at the Laboratories.

Anti-gonococcal serum has been recommended quite recently by French authors for the local treatment of gonococcal rheumatism. It is their practice to replace the synovial fluid by the serum in the large joints affected and, if need be, to give gonococcal serum subcutaneously or intravenously to prevent the extension of the disease to other joints.

Recent work in Finland has shown that the serum treatment of soft sore is effective in arresting the

disease. Up to the present we have not attempted the making of this serum in the Institute, but we hope to be able to do so at an early date.

In addition to these standard sera we have been asked to make autogenous serum for the treatment of an individual case. This is exceptional and is only of value in very chronic cases, for the immunization process is, as a rule, fairly long. If horses are available which have been immunized against some organism closely related to the one infecting the patient, the immunization can be carried out quickly and effectively.

#### Anthrax Serum.

During the last three years a few cases of anthrax due to shaving brushes have been reported in Australia, in addition to a number of cases reported as having arisen from industrial pursuits. Moreover, anthrax outbreaks in animals are not infrequent.

We have therefore commenced to examine the anthrax vaccines at present on the Australian market, with a view to the isolation from them of attenuated anthrax strains to ascertain whether the degree of attenuation corresponds to that recommended in any of the standard methods of production.

Since the immunization of the horse against anthrax takes about four months, it is improbable that any great supply of anti-anthrax serum will be available for some time.

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#### A WORD ABOUT URETHRAL IRRIGATION.

By J. Forbes Mackenzie, M.B., Ch.B.,  
Honorary Surgeon, St. Vincent's Hospital, Melbourne.

Throw a ping pong ball into a playing fountain of water and the ball will ascend to the peak of the jet and remain almost stationary there. It affords good sport in many shooting galleries.

Does the posterior urethra or the owner of one get any sport from the macroscopic and microscopic débris, laden with a precious cargo of cocci, which is squirted into the urethra with the stream of irrigating fluid? Does this débris come back with the neatly arranged return stream? Remember the water of the fountain after its ascent returns to its basin; but the ping pong ball remains at the peak of the jet. This seems a childish thing to write about in these days, when everyone who writes books or reads them, is convinced that there is only one treatment for gonorrhœa.

The sufferer from this complaint, however, who in many cases is let loose at a clinic with an irrigating apparatus, must sometimes wonder if everything is all right. He often times has had little or no instructions in its use and has to pick up the idea of it. He is not warned of the dangers of improper use and, sad to say, often becomes a regular attendant for months and months.

We are cautious and rightly so about irrigating and douching the female patient with an infected endometrium, knowing the danger of forcing infective material into tubes or peritoneal cavity. Everyone has probably seen acute abdominal pain following douching and sometimes the onset of acute inflammatory symptoms.

Should we not reconsider this irrigation method of treating urethral disease? It is, to my mind, a method which scores chiefly by its moral effect on the patient, who is more ready to pay for what he considers to be good and active treatment. The urethra will drain

itself if allowed to, but will not if allowed to settle at its outlet into a nest of pus saturated wool.

Free drainage—not free irrigation—is the treatment to aim at.

Many fellow practitioners may be absolutely satisfied with the results of their irrigation treatment of gonorrhœa. I do not know.

I only mention what appears to be the danger of irrigation. It has been mentioned before, often, but I am convinced that the method will eventually be abandoned; the sooner, the better.

#### Reports of Cases.

##### EPITHELIOMA OF THE HAND, WITH TENDENCY TO SPONTANEOUS CURE.

By C. E. Corlette, M.D., Ch.M. (Syd.), D.P.H. (Camb.),  
Honorary Surgeon, Sydney Hospital;  
and  
Keith Inglis, M.D., Ch.M. (Syd.),  
Pathologist, Sydney Hospital.

The patient, R.L., aged 63 years, a male, was admitted to the Sydney Hospital on March 16, 1920, complaining of a "sore hand," which had been troubling him for nine months.

The family history contained nothing of aetiological importance.

*Previous illnesses.*—He had had pneumonia four years previously. He denied that he had had venereal disease.

*Present illness.*—Nine months ago the patient noticed a small sore on the dorsum of the left hand, near the metacarpo-phalangeal joint of the middle finger. It increased in size and then suppurated. The sore was treated and the centre healed, leaving a ridge at the margin. This ridge continued to advance, the centre healing as the periphery extended.

*Condition on Admission.*—There was a raised, crescentic area on the dorsum of the left hand, spreading from the base of the thumb across the hand, just below the wrist joint and ending near the base of the ring finger. It was purplish in colour, with glazed skin, except on the margin facing the healed central area. Here it was rough, irregular and almost horny. No moist areas were to be seen. It was not attached to the deep structures and was not painful. There was no glandular involvement. The area enclosed within this crescentic ridge appeared to be healed scar tissue and had apparently been traversed by the growth now constituting the crescentic area mentioned.

Fifteen years ago the patient had been in the tropics (seaman), but he had not been there since.

The temperature was normal.

On March 19, 1920, the blood serum was examined by the Wassermann test with a negative result.

On March 20, 1920, a microscopical examination of the serum from the raised area was carried out with dark ground illumination. No spirochetes were seen. Blood from the raised area contained red blood cells and a few polymorpho-nuclear leucocytes and lymphocytes.

Further examination was made on March 23, 1920. No bacteria or other parasites were detected in smears from a surface scratch of the raised area and from the tissue deep in the lesion. The Wassermann test was repeated, but no reaction obtained.

Two days later a snipping was removed for histological examination. The appearances were suggestive of epithelioma.

*Operation.*—An operation was performed on March 31, 1920. Incisions were made surrounding the tumour from the base of the fifth to the base of the first digits. The tumour was then freed by dissection and removed. A large, raw area was left on the dorsum of the hand and from this area skin and fat were removed. Two parallel incisions were then made along the anterior abdominal wall and a rectangular piece of skin and fat was raised from the underlying tissues, thus forming a sleeve into which the hand was inserted. The raw area on the hand was approximated to the inner surface of the sleeve and stitched to it. The



fingers were stitched to the abdominal wall and the arm strapped to the side of the body.

On April 17, 1920, the skin flap was cut through at both ends.

On April 19, 1920, the hand was completely detached from the abdomen. The graft took well and the patient made an uninterrupted recovery.

#### Histology.

Sections of the raised crescentic area show great overgrowth of surface epithelium, masses of which project upwards and account for the raised area already described. In places there is excessive keratinization of the superficial layers of the thickened epithelium. From the deep aspect of the thickened zone downgrowths of epithelium are very obvious, though they do not extend deeply.



FIGURE I.  
Before Operation.

Isolated oval masses of epithelial cells, with keratinized centres (cell nests), which have definitely lost contact with the surface epithelium, are seen in the section. In the area of skin surrounded by the raised margin, the epithelial layer seems to be normal, the subcutaneous tissue containing an excess of fibrous tissue, except in a few places where there are slight projections on the surface and here the surface epithelium is thinned out and the connective tissue is somewhat myxomatous.

No signs suggestive of fungus or bacterial invasion are present, though collections of lymphocytes and plasma cells are conspicuous in the connective tissue stroma, especially in the neighbourhood of the epithelial downgrowths.

In the microphotograph only a small area of a depression in the surface comes into view at the upper part of the picture. The excess of keratin is well seen.

In sections stained by Levaditi's method no spirochaetes are detectable.

The condition presents the histological appearances of an epithelioma of low grade malignancy.

#### Comments.

The case here described is interesting, both on its surgical and on its pathological side. Clinically, such a case presents an extremely difficult problem for diagnosis and there arises an equally difficult problem regarding treatment. The clinical history was such as to induce a diagnosis of some kind of infective granuloma and to exclude epithelioma. Apart from the history, the physical appearances would permit the diagnosis of epithelioma, but the points were too equivocal for a definite opinion. There was a rough and irregular raised mass, but without induration and without ulceration. There could, on the history and general appearance, be



FIGURE II.  
Four Months after Operation.

no room for any doubt that the original lesion had begun on the skin near the metacarpo-phalangeal joint of the middle finger; while it had spread peripherally in a proximal direction, it had not spread distally and as it extended peripherally it healed centrally, doing so without destruction of the skin that had been the site of the lesion and without any signs of implication of the tissues beneath the skin. The skin that had healed certainly had a different appearance from that on the back of the other hand, being more dusky and more papery, apparently from the presence of a mild degree of cicatrization. Obviously, such a history is unlike that usually associated with epithelioma and, on it, few would hesitate to reject such a diagnosis. But a small piece excised for microscopical examination showed that, however atypical its clinical history, it was in its histological features apparently an epithelioma.

Next to consider was the question of treatment. Should the corresponding glands be extirpated? Should the hand or more than the hand be amputated? In any ordinary case of epithelioma of the whole of the back of the hand, with a nine months' history, there would be no difficulty in deciding. But this was a very extraordinary case, quite aberrant from type, and affected tissues had actually recovered from the disease. In view of the special circumstances, the risk seemed worth taking. The glandular area was left alone and the limb was not condemned to amputa-

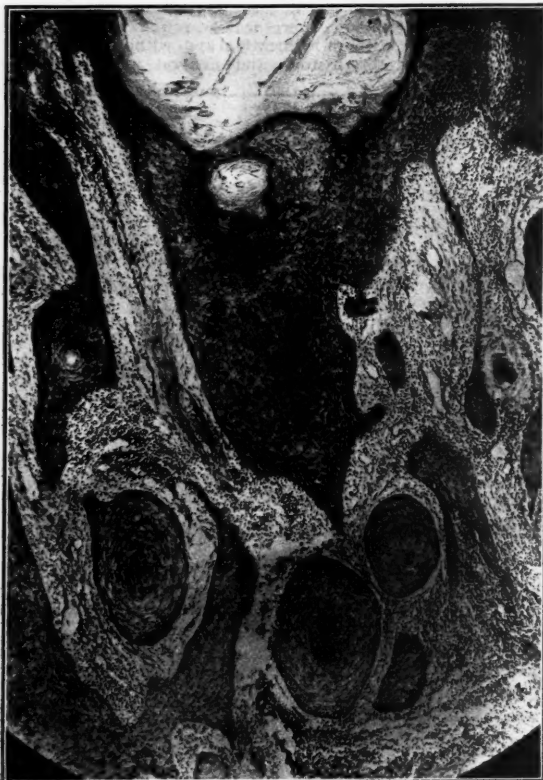


FIGURE III.  
Section of Raised Crescentic Area ( $\times 52.5$ ).

tion. But, of course, the whole of the diseased area had to go. The re-covering of the denuded surface on the back of the hand was the next problem. This was solved by the grafting expedient that has been described. The patient had an obese abdominal wall and though the fatty layer was trimmed away from beneath the skin till it seemed fairly thin, the result shows that more could have been removed with advantage, since the new covering of the back of the hand has too thick a pad of underlying fat and this impairs its appearance.

## Reviews.

### WORK IN THE CLINICAL LABORATORY.

"Diagnostic Methods," by Ralph W. Webster is, as the author points out, a book for students and practitioners.<sup>1</sup> The field covered is so vast and varied that some of the subjects dealt with can only be touched upon in a work of

<sup>1</sup> Diagnostic Methods, Chemical, Bacteriological and Microscopical: A Text-Book for Students and Practitioners, by Ralph W. Webster, M.D., Ph.D.; Sixth Edition, Revised and Enlarged; 1920. Philadelphia: P. Blakiston's Son & Company; Royal 8vo., pp. 844, with 37 coloured plates and 170 other illustrations.

this type. The bibliography is extensive and well arranged, so that reference to original papers for greater detail is made easy. The illustrations are numerous, but, on the whole, are not quite up to the standard of most modern works. The coloured plates, in particular, are only moderately good. Chemical methods are given greater prominence than are microscopical and bacteriological procedures.

The book is divided into eleven chapters dealing respectively with sputum, oral, nasal, aural and conjunctival secretions, gastric contents, parasites, feces, urine, secretion of the genital organs, blood, transudates and exudates, secretion of the mammary glands and clinical bacteriology. The chapter on urine occupies 216 pages, of which the first 176 are devoted purely to chemistry. In Chapter XI, under the heading of clinical pathology, the author deals with apparatus, sterilization, preparation of media, incubation, preparation of cultures, staining, identification of organisms and vaccines, the whole being condensed into 33 pages.

The book includes quite a number of new methods from the laboratory of Folin, such as Folin and Bell's direct nesslerization method for ammonia in urine; Folin and Denis's direct nesslerization method for total nitrogen in urine and their method for the estimation of lactose in milk; Folin and McEllroy's test for sugar in urine; Folin and Peck's quantitative tests for sugar in urine; Folin and Wright's simplified Kjeldahl method; Folin and Wu's system of blood analysis, which includes methods for the determination of creatin and creatinin in blood, non-protein nitrogen in blood, sugar in blood, urea in blood, uric acid in blood and uric acid in urine; Folin and Youngburg's direct nesslerization method for urea in urine. The subject of functional renal diagnosis has been enlarged and a discussion of Mosenthal's test meal for renal function has been included. The section dealing with the reaction of the blood has been entirely rewritten, to bring it up to the present-day conception of hydrogen-ion concentration.

In the discussion of the parasitology of the blood the subject of infectious jaundice has been introduced, a full account of the *Leptospira icterohæmorrhagica* (Noguchi) being given. In the section on clinical bacteriology the discussion now includes the gas bacillus of Welch, which assumed considerable importance in the study of wound infections during the war. No mention is made of *B. œdematiens*, *Vibrio septique*, *B. sporogenes* and other anaerobes which have recently come into prominence. Indeed, the anaerobes are given but scant attention, whereas relatively unimportant organisms, like the Koch-Weeks bacillus and the Morax-Axenfeld diplobacillus are illustrated with coloured plates. No reference is made to the work of Weinberg, Henry Bull, Miss Robertson and others who, during the war, greatly advanced our knowledge of anaerobic organisms and methods of investigating them.

### THE MANAGEMENT OF DIABETES.

The second edition of Joslin's "Diabetic Manual," as might have been expected, has not been long delayed in its appearance and, with very little alteration in the text, is the same valuable aid to both physician and patient in the treatment of this all-too-prevalent disease. The book is essentially for the use of the patient. An endeavour has been made to simplify it to some extent, in order to increase its value.

Joslin states that "for one diabetic patient who learns too much about the disease, there are unquestionably ninety-nine who know too little." This book will give the patient all he needs to know about his disease and, if of average intelligence, he will have little difficulty in following the simple directions set forth.

We commend it to every practitioner who has to treat a patient with diabetes. If trouble be taken to master the contents, little difficulty will be experienced in managing the patient successfully in the great majority of cases.

The book is a small one of less than 200 pages, beautifully printed in large type, well illustrated and can be read easily in a very short space of time. It will repay the reader for any trouble taken to master its contents.

<sup>1</sup> A Diabetic Manual for the Mutual Use of Doctor and Patient, by Elliott P. Joslin, M.D.; Second Edition; 1919. Philadelphia and New York: Lea & Febiger; Deny 8vo., pp. 191, illustrated. Price, \$1.75.

## The Medical Journal of Australia.

SATURDAY, MARCH 26, 1921.

### Therapeutic Sera.

A few years ago the Federal authorities invited Dr. W. J. Penfold to organize and manage the new Commonwealth Serum Laboratories. In the special line of establishing and directing an institution of this kind, Dr. Penfold was an untried man. He was well known as a sound bacteriologist and his researches conducted for several years at the Lister Institute of Preventive Medicine had won for him a reputation as an expert scientific worker in many branches of his specialty. In this issue we publish an article from which it will be gleaned that the choice of the Director of the Commonwealth Serum Laboratories was a wise one and that the advisers of the Federal authorities had taken no risks in recommending the appointment of Dr. Penfold. The Federal authorities have not exhibited the same amount of judgement nor of sense of proportion in their determination to introduce the principles of protection into the commercial activities of the new institution. Dr. Penfold claims that the imposition of a heavy impost on imported sera and bacteriological products has inflicted no damage on the Australian people. He is the last man to express such an opinion, since his own products are those which have benefited by this tariff. There is only one reliable test of efficacy—comparison. We have no doubt that if the Commonwealth Serum Laboratories are given a chance to compete on fair terms with the other great serum institutions of the world, its products will rank high. We learn from Dr. Penfold that in the laboratories attached to almost all of the leading firms and serum institutes some secret method is being used. The commercial aspect of the production of sera has been developed as well as the scientific. The visitor to these laboratories is shown much, but not all of the technical details of the work. The fact that Dr. Penfold has taken out a patent for his own method of returning the red blood corpuscles into the horse after bleeding, so as to increase the

yield of serum, is evidence of the truth of this statement. Dr. Penfold does not derive any material benefit from his patent; the benefit accrues to the Commonwealth Serum Laboratories. But the letters patent are intended to prevent competing firms from using this technical improvement without buying the right to do so.

Therapeutic sera are not ordinary articles of commerce. They are used in the treatment of serious disease and on their efficacy the life or death of an Australian citizen may depend. For the rich man the increase in price of the imported articles is of no moment. The additional cost may place a given product out of the reach of the poor man. While these remedies are prepared with the aid of secret processes all over the world, it is obviously impossible to substantiate the claim that the sera produced at the Commonwealth Serum Laboratories are the best obtainable in every case. The Minister for Trade and Customs is prepared to make the rich pay in money and the poor in lives. Protection may be a wise policy in regard to ordinary goods; in the case of therapeutic sera it savours of inhumanity.

### THE TREATMENT OF WOUND INFECTIONS.

The subject of the nature of wound infection in warfare attracted the attention of surgeons and bacteriologists almost from the moment the forces took the field in 1914 until the signing of the armistice. An immense literature has arisen; so immense, that some of the more valuable contributions to knowledge of the subject have been lost among the vast volumes of useless speculation and unproven opinions. The opportunity for sound, scientific investigation and for careful observation was almost limitless. At the same time there was a feverish anxiety among a certain class of worker to make epoch-making discovery and a consequent tendency to take short cuts to fame. It is doubtful whether the harvest of scientific results has been commensurate with the amount of experiment or with the mass of published articles. Many new antiseptics of reputedly high value in addition to old antiseptics in new form have been vaunted in an imaginative and exaggerated manner. The modern list of antiseptic substances that may be applied to wounds is so large that the student may become confused. A critical survey of the work, however, soon reveals that much of it represented a competition between the protagonists of direct chemical action and those of mechanical or biological means of cleansing wounds. The bacteriology of infected wounds in France, Egypt, Palestine and the other theatres of the war has been well worked out and may be regarded as a more or less closed chapter. Some of this work has a direct application to the conditions of



civil practice, while in other respects the nature of the contaminating bacteria has a practical bearing limited to military surgery. The much delayed publication of the results of a prolonged study of infected wounds undertaken in 1916 by Drs. S. R. Douglas, A. Fleming and L. Colebrook<sup>1</sup> reaches the medical profession at a time when the bitter controversies are almost forgotten. The contribution represents the results of bacteriological investigations undertaken in Almoth Wright's department at St. Mary's Hospital in London and clinical observations carried out in a ward set aside for the purpose in the same institution. That the views expressed by these workers should coincide to a very large extent with those initiated by Sir Almoth Wright is scarcely surprising. The first and second parts of this report cannot be dealt with at present. They contain an account of the way in which the research was conducted, the results claimed from the employment of certain splinting material, of methods aiming at the reduction of pain during the dressing of the wounds, of massage and vaccines as agents for the promotion of healing and similar matters. The bacteria found in the wounds are minutely described.

In the third part the authors attack the problem of the value of certain antiseptics and of hypertonic salt solutions in the treatment of infected wounds. They set up the following properties as essential for an ideal antiseptic. It must be capable of killing bacteria in the discharges of the wound, of penetrating into small diverticula, of permeating the walls of the wound in order to kill the bacteria entrenched in this situation. It must not exercise any destructive action on the tissues of the wounded part nor interfere with the physiological properties of the tissues or cells and it must not exert a general toxic effect on the patient. Two patients with large cup-shaped wounds were selected for this study. Antiseptics were introduced into these wounds for varying periods of time. After the period had elapsed, samples of the fluid were mixed with melted agar and the mixture allowed to solidify prior to incubation. It was found that the number of colonies remained unaltered by the introduction of Dakin's solution acting for one or two hours. When eusol was employed the number of colonies reached a maximum after 20 minutes and then became reduced. The authors express the conviction that this reduction could not have been caused by the antiseptic action of the hypochlorite. No appreciable effect was determined when chloramine T was employed, while the results with flavine were inconclusive. In the next place they endeavoured to ascertain why these antiseptics failed to sterilize the wounds. Samples of the antiseptic were withdrawn from the wound at regular intervals and tested to determine the concentration. It was found that Dakin's solution, eusol, chloramine T and flavine all underwent rapid destruction when in contact with living tissue. For example, when eusol representing 0.4% of hypochlorite was introduced into the wound, the strength of the fluid in the wound had diminished to under 0.1% after five minutes and to about 0.04% at the end of ten minutes. This loss of free antiseptic in solution

was found to be greatly increased when gauze or cotton wool is used as a dressing on account of the fixation of a relatively large amount of the dye by the fabric. Further experiments were undertaken to ascertain the effect of varying concentrations of antiseptics on bacteria suspended in serous fluids. The authors found that the weakest concentration necessary to kill all the bacteria within a given time was higher than the concentration of the antiseptics when applied in ordinary strength and left in contact with the wound tissues for the same length of time. Moreover, they discovered evidence of a stimulating action on the growth of bacteria *in vitro* when certain antiseptics were used in a concentration equivalent to that found when the ordinary solution has been in the wound for five minutes. They further examined the effect of several antiseptics on the leucocytes. In all cases they discovered a destructive effect on the leucocytes of weaker solution than are needed to exert a bactericidal action. In the last place they investigated the influence exercised by antiseptics on the antitryptic power of serum. The growth of gas-forming bacteria in serum was determined when varying quantities of trypsin were added to the serum culture. It was found that gas formation took place at an increasing rate, as the antitryptic power was diminished and reached its maximum in the presence of free trypsin. No gas formation occurred when the antitryptic power approached the normal. The addition of eusol, Dakin's solution or flavine resulted in a considerable reduction of the antitryptic power of the serous fluid. They consequently arrived at the conclusion that antiseptics were not only useless in the treatment of infected wounds, but were actually harmful. The concluding part of the report contains the record of experiments with hypertonic salt solution which they believe to be capable of increasing the quantity of exudate produced in the wound, of enriching its albuminous content and of encouraging an emigration of undamaged leucocytes in the wound cavity.

It is impossible within the compass of a short article to give the details of the experimental work undertaken by these investigators. Much of the work is open to criticism. They have attacked a somewhat complex problem from a definite aspect and have fitted their experiments to the views which they hold on the processes involved. We may instance a series of experiments designed to disclose the effect of antiseptic in wound pockets. The conditions of the experiments were so unlike the conditions of a real wound that their conclusions cannot be accepted in the absence of further evidence. Again, the measurement of an alleged antitryptic action of the serum on the growth of bacteria does not bear any direct relation to the question at issue. They have actually touched the question of the adsorption of certain antiseptic substances by other bodies without revealing an understanding of the laws governing adsorption. Antiseptic action is primarily a chemical one. The authors have considered it from the view of a physical process. Their work is interesting and important and much of the data advanced will be valuable when the problem is attacked in a different manner. It is not improbable that the commonly used antiseptics exercise a deleterious

<sup>1</sup> Studies in Wound Infections. Special Report Series, No. 57, Privy Council, Medical Research Council, 1920.

effect on the tissues and tissue fluids more damaging than the action of bacteria growing on the surface of an open wound. It would seem, however, that the nature and virility of the bacteria in the wound are important factors to be taken into account. Surgeons will probably not be content to give up the use of antiseptics for wounds in favour of hypertonic salt solution unless more convincing arguments are adduced.

#### GRAM'S STAIN.

The majority of bacteriologists use Gram's method of staining as a convenient means of distinguishing two groups of bacteria, those which retain the stain—gentian violet or some other pararosaniline and iodine—after treatment with alcohol and those which become decolorized in the process of treatment with alcohol. While they recognize that at times partial or unequal decolorization takes place, they scarcely trouble themselves with the phenomenon which they use as an arbitrary means of differentiation. It has long been known that stains and dyes may impart their colour to a material either by absorption or adsorption without any chemical combination or by entering into chemical union with a constituent of the material offered for staining. The true chemical reactions are often but not always characterized by a change of colour. It has been shown that the true chemical combinations in histological staining are more specific than the purely physical phenomena. In the staining of cells and their contents there frequently exists a special affinity on the part of a constituent for a constituent of the stain; the attraction is physical, but there may follow a chemical reaction when the two substances are brought into close relationship. Gram's staining method has, at first sight, the appearance of being an instance of a physical staining changed into a chemical dyeing by the action of a mordant. Another possible explanation that has been put forward is that the pararosaniline dyes enter into a chemical combination with iodine and the protein of the bacterium and that the resultant compound is relatively insoluble. As this view failed to provide an explanation for the retention of the stain in some bacteria and not in others, it was suggested that the compound depended on a lipid. This hypothesis gained in favour when it was shown that the so-called Gram-positive bacteria contain a lipid substance and further that Gram-positive bacteria from which the lipid has been extracted, no longer manifest the ability of retaining the pararosaniline dye. Further support has been gained from the discovery that Gram-negative bacteria which have been treated with emulsions of lecithin, tend to retain Gram's stain. If this were the true explanation of Gram's staining, it would be necessary to ascertain the biological significance of lipid in the cell body. It would be of much greater importance if the reaction were found to be indicative of a real biological difference between the two groups of bacteria than if the reaction proved merely to be a convenient means of distinguishing them on physical grounds. Dr. T. H. C. Benians has undertaken the study of the phenomena involved in this method of staining and has thrown some light on it.<sup>1</sup> In the

first place he found that when staphylococci, gonococci and *Bacilli coli* were emulsified in a solution of gentian violet or Victoria blue, the first two abstracted the stain from the liquid and became intensely coloured, while the colon bacilli remained unaffected. Preliminary heating of the colon bacilli to 65° C. for half of an hour caused them to take up and retain the dye. This did not occur when the bacilli were killed by heating to 60° C. The heating to the higher temperature obviously causes a physical change in the cell wall, probably a coagulation of the albumin. Dr. Benians refers to the fact that heating to 65° C. produces a profound change in the antigenic and agglutinin-forming properties of the coli-typhosus group of organisms. He is inclined to interpret this set of experiments as indicating that one explanation does not suffice for the phenomenon of the failure to take up and retain the stain on the part of Gram-negative bacteria. In some the stain permeates the cell, while in others it does not penetrate the cell wall. He then examined the solubility of the Gram compound in the bacterium. Methyl-violet and iodine in the test tube are less soluble in dilute alcohol than in absolute alcohol. Staphylococci and debris of this organism were fixed on slides and stained with methyl-violet and iodine. The films were dried and treated in one case with absolute alcohol and in another with 80% alcohol. The cocci treated with absolute alcohol retained the stain, while the debris were decolorized. Decolorization occurred both with the cocci and with the debris when 80% alcohol was used. Further experiments revealed the fact that when bacteria were broken up and the amorphous debris stained by Gram's method, the distinction between the Gram-positive and the Gram-negative was lost. Retention of the stain by the debris was feeble, although the material took up the dye before washing in alcohol more readily than the intact bacilli. He produces evidence to show that the cell bodies of the bacteria do not contain anything that exercises a specific chemical affinity for the compound stain. He, therefore, holds that the phenomenon of Gram's staining is governed by the physical structure of the cell and is probably dependent on the nature and integrity of the limiting membrane. In the case of Gram-positive bacteria he assumes that this membrane does not permit the large compound dye-iodine molecule in alcoholic solution to pass through it. He suggests that when weak alcoholic dilutions are employed, the imbibition of water alters the permeability of the membrane. In regard to the so-called Gram-negative organisms, he offers the following explanation. In one group the cell possesses no limiting membrane. The dye passes readily into it, but is just as readily removed by alcohol. In the second group the dye is merely adsorbed on the surface of the cell, from which it can be removed by washing in alcohol. According to this explanation, the behaviour to Gram's method of staining depends on physical factors, but these again probably have a biological significance. We still require to know the function of the lipid or other constituent which imparts to the cell-limiting membrane the physical character necessary for the retention of the dye-iodine compound despite washing with alcohol.

<sup>1</sup> The Journal of Pathology and Bacteriology, December, 1920.

## Abstracts from Current Medical Literature.

### ORTHOPÆDIC SURGERY.

#### (110) The Operative Treatment of Infantile Paralysis.

The surgeon who treats paralysis of the lower limbs, takes a novel and rather peculiar view of the requirements of human activity. In this scale of requirements he recognizes three essentials: (1) That the patient should be able to stand on his feet and progress in some manner or other; (2) that he should be able to get up and down out of a chair; and (3) that he should be able to go up and down stairs. In regard to the treatment of patients who cannot walk, Robert W. Lovett (*Surg., Gynec. and Obstet.*, January, 1921) contends that any patient of average intelligence with flaccid paralysis of the lower extremities, abdomen and back can be made to walk in some form or other, provided he has one good arm and one good enough to hold a crutch. The most common obstacle to putting a patient on his feet is contracture of the hip in flexion. This may be remedied by Soutter's operation (fasciotomy with detachment of the muscles surrounding the anterior superior spine of the ilium) or, in milder cases, by continuous stretching. Permanent flexion of the knee may prevent walking and is to be treated by gradual stretching. *Equinus* deformity of the foot is the third deformity which, if existing in both legs, makes walking practically impossible. In the treatment of this deformity tenotomy should be used with extreme caution. The contracture will in most cases yield to gradual stretching. After correction of the deformity the patient should be instructed in tripod walking. Crutches form the two anterior legs of the tripod, while the third and posterior leg is formed by the body of the patient inclined forward at its upper part with the feet well behind. Hyperextension at the hips is checked by the ilio-femoral ligament, the knees are held in splints and the weight falls in front of the hip joints and enables the patient to stand upright. The power of progression can be acquired. The most interesting and important problem in the treatment of infantile paralysis is that of improving the walk of those patients who are able to move about. In dealing with lameness the surgeon should carefully examine the abdominal and gluteal muscles. Correction of deformity in the feet will not greatly improve the patient's condition if these muscles are paralysed. The limp caused by paralysis of the gluteal muscles cannot be concealed or remedied by any apparatus, but is minimized by the use of a strong elastic band. Abdominal paralysis is much more common than has generally been supposed. The complicated limp may be minimized by wearing a well-fitting corset. In the treatment of deformities due to paralysis, tendon transplantation

has been successfully employed by the author, more especially by fixing the *extensor hallucis longus* tendon to the first metatarsal bone in cases of mild *valgus* deformity and by transferring the *peroneus longus* tendon to the medial side of the foot and by insertion of the *tibialis posterior* and one of the peroneal muscles into the *os calcis* in cases of *talipes calcaneus*. Tendon fixation has been proved to be satisfactory, although occasionally the tendons were stretched or pulled out of their attachments. Silk ligaments have been discarded. Atragalectomy when performed after the age of fourteen years is a good operation, but in young children the astragalus should only be removed in cases of severe calcaneus deformity. In cases of paralysis of the upper limb the minimum requirements for a successful operation are, firstly, power of flexion of hand and fingers and, secondly, ability to move the scapula on the thorax. Arthrodesis of the shoulder is the best procedure when there is paralysis of the deltoid. In the hand tendon transplantation is often of use, particularly for the improvement of the movements of the thumb.

#### (111) Reduction of Old Dislocation of the Hip.

Traumatic dislocation of the hip joint must be considered old at the end of four weeks. After this time the acetabulum becomes filled with connective tissue and fringes of the torn capsule which present an effective bar to reduction. From an examination of the literature, J. J. Buchanan (*Surg., Gynec. and Obstet.*, November, 1920) comes to the conclusion that an open operation is the only reasonable line of treatment. One case is reported. The patient was a young man and the operation was undertaken seven months after the accident. As a preliminary treatment, extension was applied to the shortened limb, but only produced about 1.3 cm. additional length. At the actual operation the cavity of the acetabulum was found to be roofed over and filled with dense connective tissue. This tissue was dissected out until the normal cartilage appeared. The head of the femur had to be freed from a bed of connective tissue by the use of curved scissors passed behind the bone. Four levers were then placed under the neck and by their use and with the aid of an assistant, who provided efficient manipulation and traction, the head was delivered into the acetabulum. The limb was fixed in the position of abduction with slight traction. The result was satisfactory and the patient walks without pain, though there is limitation of movement in all directions.

#### (112) The Treatment of Fractures.

H. Winnett Orr (*Journ. Orthop. Surg.*, January, 1921) criticizes the present treatment of fractures and deplores the inaccuracy and adherence to old methods of many of the recent text books. The following conclusions he considers are justified by experience in military hospitals: (i.) There are two agencies

of major importance in the treatment of fracture of the femur and the leg. These are Thomas's splint and plaster of Paris. (ii.) The less Thomas's splint is modified, the more efficient it is. (iii.) For fracture of the neck of the femur, as shown by Whitman, and for fracture of the leg below the knee, either open or closed, plaster of Paris is usually indicated. (iv.) For fracture of the shaft of the femur Thomas's traction splint is the most useful device, both for emergency use and for continuous treatment. (v.) Skeletal traction for fracture of the extreme lower end of the femur or leg is a justifiable addition to Thomas's splint. (vi.) The Balkan frame and the Hodgen's splint in a few instances may be applied for the treatment of extensive compound injuries of the thigh. The author also believes that too little stress is laid on immobilization, stiffness, excess of callosities, adhesions and ankylosis are all due to failure in adequate fixation. Ideal immobilization from the beginning would lead to healing of joint injuries with a minimum of joint damage.

#### (113) Traumatic Dislocation of the Knee Joint.

The advantage of complete and prolonged immobilization of the knee joint after complete dislocation is illustrated in a case reported by Harry Platt (*Brit. Journ. Surg.*, October, 1920). The patient was a man, aged 47 years, and the injury was caused by striking the knee on a plank while falling from a ladder. Reduction presented no difficulty. The patient left hospital in seven days with the knee immobilized in plaster and was walking comfortably when the casing was removed four months later. The joint was quite stable, but had only about five degrees of movement. A caliper splint was then applied and work was resumed seven months from the time of the accident. The range of movement gradually increased and at the end of eleven months twenty degrees of flexion were present. Stability remained unimpaired and there was no sign of injury to the crucial ligaments. Four years after the accident the patient could produce more than 90° flexion and the stability was perfect. The author suggests that prolonged immobilization gives stability in injuries of the crucial ligaments more readily than in a case of complete dislocation. Mobility should be sacrificed for stability.

### MORPHOLOGY.

#### (114) The Earliest Stages in the Human Clavicle.

Frank Blair Hanson, writing in the *Anatomical Record* (November, 1920), remarks that the clavicle is one of those elements of the human skeleton concerning which the last word has not yet been spoken. Since the days of Gegenbaur, in 1864, an enormous mass of literature has arisen, most of which would be of historic interest only, were it not that Huntington, in 1918, at-



tempted to restore the old hypothesis of a cartilaginous precoracoid core in the human clavicle. Hanson has tried to determine whether the origin is in cartilage, or in an element of the dermis, or whether the clavicle is derived in part from both cartilaginous and membranous elements. As a result of his studies of the unique collection of cleared specimens from human embryos (upon which Mall based his paper on ossification centres), as well as the collection of serial sections in the Carnegie Laboratory of Embryology, Hanson states that ossification begins about the thirty-ninth day and arises in two distinct centres, one in the lateral half and one in the medial half of the clavicle. At this time the bony centres are surrounded by "peculiar precartilaginous tissue," which is certainly not hyaline cartilage. It seems quite clear that the earliest stage of ossification in the clavicle, both in medial and lateral halves, is a dermal ossification and that cartilage is entirely lacking at the time of the appearance of the two centres of bony tissue. The precoracoid has a history so different from that contemplated by those who see in the cartilage the old precoracoid, that this cartilage could not possibly be that element. It has been shown in marsupials that there are two coracoid elements in the shoulder girdle, of which the posterior is comparable directly with the coracoid of monotremes. This becomes the small rudimentary coracoid process of the scapula in the adult and this process is undoubtedly homologous with this process of the same name in man. A clear line of genetic relationship is traceable from the coracoid process of man to the posterior element in the girdle of monotremes. The latter is comparable with the posterior of the two coracoids in sphenodon and lizards, which, in turn, is a derivative of the precoracoid of Permian reptiles. Thus the coracoid process of man is the equivalent of the anterior bony element of Permians and the precoracoid is the true coracoid. In marsupials the fully formed clavicle and precoracoid are co-existent and separated by a considerable space. There is therefore, no way in which the cartilage of the precoracoid can enter the clavicle in mammals. The final conclusion, then, must be that there are very solid grounds for considering the human clavicle to be a purely dermal bone.

#### (115) Crossed Displacement of the Left Kidney.

C. M. Wilhelmj gives details of an anatomical specimen in which the left kidney lies on the right side of the body, below and medial to the right one, with presumably some degree of fusion between the two (*Anat. Record*, March 20, 1920). The right or normal kidney lies abnormally low in the abdomen, its lower pole extending 2.5 cm. below the iliac crest. The left or displaced kidney lies below and medial to the normal one and overlaps slightly the right common iliac artery. The vessels of the normal right kidney pre-

sent no marked peculiarities. Two arteries supply the displaced viscus. The upper arises from the aorta on the left side at the level of origin of the inferior mesenteric artery and passes behind the inferior mesenteric vessels and in front of the aorta to reach the hilus of the displaced kidney. It is accompanied by the large left renal vein, which arises from the *vena cava inferior* at the normal level, crosses in front of the aorta to the left side, turns downwards and curls below and behind the inferior mesenteric vessels, recrossing the aorta at the same time. The pelvic vessels are also of interest. There is no right common iliac vein and the right hypogastric (internal iliac) vein joins the left common iliac vein. The ureters, although displaced, join the bladder in a normal fashion. A discussion of the previous literature on the subject is given. McMurrich's view in similar cases is that the kidney has in some way been retarded in its upward migration. When an organ has failed to migrate at the proper time, it is at once subjected to the influence of adjacent organs which under normal conditions would not have affected it. In the case of a retarded kidney at least three such foreign influences may play a part in its displacement. The first influence is the rotation of the gut when it begins the assume the adult position. The second is the great increase in size of the caudal end of the Wolffian body, which would not affect a normal kidney because the latter would have migrated towards the cranial end of this organ, which is already undergoing degeneration and decreasing in size. The third and last influence is the descent of the sex gland. The only conclusion reached by the author is that the displacement occurred before the rotation of the intestine, since the left ureter crosses behind the pelvic colon, while the renal vessels supplying the displaced kidney pass behind the inferior mesenteric artery. Finally, the possibility of the derivation of abnormal renal veins from embryonic venous channels is discussed in detail.

#### (116) The Development of Taste Buds.

J. M. D. Olmsted in discussing the nerve as a formative influence on the development of taste buds, remarks that the influence of one organ upon the development of another is a fundamental problem in morphogenesis (*Journ. Compar. Neurol.*, June, 1920). Embryologists have rather taken for granted that the differentiation of specialized organs, such as the transformation of epithelial cells into taste buds, is due to the growth of the appropriate nerve into the region concerned. This author brings forward additional evidence that the presence of the nerve is the formative influence in the development of taste buds. The material experimented on was supplied by the barbels of the catfish, *Amiurus nebulosus*, the ends of which were cut off and then the process of regeneration carefully followed through every

step. It was found that in all stages of regenerating ends of barbels the nerve and cartilage extend practically the complete distance from the old stump to the basement membrane of the epidermis at the very tip. Short regenerated pieces show no trace of taste buds. The formation of dermal papillae, the invariable forerunners of taste buds, takes place at the base of longer regenerated pieces, as if the germinated layer of the epidermis were indented by the growth into it of a small branch of the nerve trunk. Each papilla is filled with a small bundle of nerve fibres which stand out from the nerve trunk like a small button, causing this indentation of the germinative layer. Later stages show the presence of fully developed taste buds along the whole length of the regenerated end, mainly concentrated, however, along the edge nearest the nerve. Since taste buds degenerate in a barbel whose nerve is cut and reappear when the nerve regenerates and since the nerve appears in the appropriate region before there is any evidence of a developing taste bud, the presence of the nerve may be said to be the causative factor in the formation of taste buds.

#### (117) The Pre-Natal Growth of the Guinea-Pig.

R. L. Draper (*Anat. Record*, May 20, 1920) has investigated the pre-natal growth of the guinea-pig and records his observations. He finds that variations between the weights of early embryos of the same age are relatively greater than those from the later part of gestation. This variation appears to be greater than could be accounted for by errors of observation. He admits that observations become accurate only after about the 15th day. Growth occurs rapidly from the 15th to the 25th day, decreasing rapidly at first and then more slowly for the rest of the period. During the first month the weight of the membranes and placenta is greater than the aggregate weight of the embryos. At the 32nd and 33rd days they are equal in weight and from thence on the embryos gain rapidly in weight, while the membranes gain slowly. From the 25th to the 44th day a more rapid increase in growth of the membranes and placenta takes place than in the subsequent period. Once they have reached a sufficient size to meet the future demands of the embryo, there is probably no further need for their rapid continued growth. The material used in these observations consisted of 145 embryos from 48 pigs. The author also records a valuable series of observations on the breeding habits and general management of guinea-pigs. He finds that they are very susceptible to cold and sudden changes of temperature and diet. These factors frequently cause abortion and death. The most suitable temperature at which to maintain them was found to be between 16° C. and 22° C. He also has reason to believe that guinea-pigs are not as prolific as is popularly supposed.

## British Medical Association News.

### SCIENTIFIC.

A meeting of the New South Wales Branch was held at the B.M.A. Building, 30-34 Elizabeth Street, Sydney, on November 26, 1920, Dr. C. Bickerton Blackburn, the President, in the chair.

Dr. W. J. Penfold, Director of the Commonwealth Serum Laboratories, gave an account of the developments in the production of therapeutic sera in Australia and illustrated his remarks by demonstrating apparatus and by exhibiting tables and graphs on the screen (see page 245).

Professor A. E. Mills prefaced his remarks by stating that he did not feel qualified to express an opinion on the various technical points dealt with by Dr. Penfold. They were extremely indebted to him for his most interesting and informative paper. He had displayed an enthusiasm of an extraordinarily high order which compelled their admiration. He thought that Dr. Penfold need not be disappointed or discouraged because physicians at the hospitals had not taken up the treatment of pneumonia by means of the specific, typed anti-sera with which he had dealt. He had long been interested in the question of the treatment of pneumonia. The treatment adopted at the present moment appeared to him to be very unsatisfactory. They were in the habit of speaking of the expectant treatment, by which he presumed that they meant that they expected the patient to get well. There was, however, a hopeful sign in the recognition by medical practitioners that their results should be greatly improved. Unfortunately, those who saw the greatest number of patients with pneumonia were the busiest practitioners. They had little time to give an injection of 100 c.cm.. Dr. Penfold had pointed out that this injection had to be given slowly, which meant that it took a very long time. The de-sensitization, too, took a long time. He thought that these facts militated against the general adoption of the treatment. He suggested that efforts should be made to obtain a serum of high potency so that pneumonia could be treated as easily as diphtheria. Professor Mills congratulated Dr. Penfold on his original and highly ingenious work on the re-fusion of red blood cells. The process appeared to be one almost of perpetual motion.

Dr. A. H. Tebbutt congratulated Dr. Penfold on his paper and on the admirable progress which he had made. He was satisfied that few men could have developed a serum laboratory as rapidly and as efficiently as Dr. Penfold had done. His laboratories had become the finest in Australia. After a few remarks on the organization of the scientific and business side of the institution, Dr. Tebbutt referred to the question of the protective tariff. At a former meeting of the New South Wales Branch he had sided with the majority of members in protesting against the duty on imported bacteriological products and sera. He still considered that the products of the well-known firms in England and other countries should be available to the profession in Australia. It had come to his knowledge, however, that some of the imported products were not of first-class quality. It was his opinion that in the majority of instances there was no wilful wrong labelling, but that the products had deteriorated through the absence of proper storage during transport through the tropics and through inefficient methods of storage in Australia. He recommended the establishment of a laboratory under Government or British Medical Association control for the testing and standardization of all products on the market. He was sure that the serum laboratories already possessed the confidence of the profession in Australia.

In regard to Dr. Penfold's remarks on pneumonia, he agreed that treatment by specific serum would be preferable to the chance methods employed in Melbourne and Sydney. There certainly were difficulties in the administration of large quantities of serum when injected intravenously. During the past winter there had been relatively little pneumonia in Sydney. A few patients had been treated in hospital, while the greater number had probably been treated in their own homes. In New York at the Rockefeller Hospital there had been between 400 and 500

cases of all the types. The mortality had been about 25%. This was considerably higher than the case mortality in Australia. There was consequently less urgent need for specific treatment.

Dr. W. F. Litchfield added his thanks to Dr. Penfold. He thought that the use of serum in the treatment of pneumonia was of considerable importance to the practitioner. At the Children's Hospital they had used the Commonwealth serum in very large doses and had obtained satisfactory results. They had not experienced any serious forms of serum disease. Usually the reaction took the form of an urticaria. In the case of a nurse there had been an almost immediate reaction. She had become very ill, but had eventually recovered. While he recognized the advisability of de-sensitizing patients who had had serum before, he was inclined to the opinion that the risks were not so serious as many held them to be. He did not hesitate to give large doses without any preliminary measures when they appeared to be indicated. One patient had collapsed after having received 0.12 c.cm.. It was said to be less dangerous to give a massive dose than a small one.

Dr. Litchfield referred to a case of pneumococcal meningitis in a patient at the Children's Hospital. The child had received 14 injections of polyvalent pneumococcal serum intrathecally. Recovery had followed. He stated that this was the only recovery of which he had heard. He agreed with Dr. Tebbutt that the type of pneumonia recently seen in Sydney was not severe. He thought that anti-pneumococcal serum might be of considerable value in cases of delayed resolution after pneumonia.

He expressed the opinion that small epidemics of true dysentery occurred among older children from time to time in Sydney. The dysenteric nature of the colitis in these cases was definite. While he advocated treatment with anti-dysenteric serum, he admitted that the result of his experience was inconclusive. Five children had been treated with serum. There were no dramatic recoveries, but all the children ultimately did well, as did those who had not received serum. The results which he had got from the use of tetanus antitoxin had also been inconclusive. He had used this serum both intrathecally and subcutaneously. He held the opinion that the termination in these cases depended rather on the type of infection than on the treatment. When the incubation period was short, the disease was usually fatal.

Dr. C. Bickerton Blackburn, O.B.E., thanked Dr. Penfold for his very interesting paper. Dr. Litchfield had stated that pneumococcal meningitis was invariably fatal. He referred to the case of a lad aged 17 years who had had the symptoms and signs of acute cerebro-spinal meningitis. Pneumococci were recovered from the cerebro-spinal fluid. On the sixth day the temperature fell by crisis and recovery ensued. He agreed with Dr. Tebbutt that pneumonia in Sydney was not as fatal a disease as it appeared to be in America. The majority of their patients got better, but he would be glad to have a remedy to make the recovery surer. He promised Dr. Penfold to test the efficacy of Type I. serum if Dr. Tebbutt would be willing to work out the type of pneumococcus causing infection.

They had found anti-dysenteric serum a most valuable adjunct to treatment in Egypt. It was necessary, however, for the serum to be satisfactory. At one time their supply consisted of old serum that had been exposed to great heat. This serum was useless as a therapeutic agent and gave rise to severe serum sickness of rapid onset in almost every patient. As soon as a supply of fresh serum became available, the results were excellent. They had given doses of 100 c.cm. into the adductor muscles of the thigh. The serum was absorbed within a short time. In conclusion, Dr. Blackburn referred to the case of a girl of 14 who had come under his care in Sydney almost moribund from ulcerative colitis. The condition appeared very similar to bacillary dysentery. It had subsequently been shown that it was caused by Shiga's bacillus. The patient had died before the bacillus had been identified.

Dr. Penfold, in reply, stated that he recognized that the treatment of pneumonia with the typed anti-pneumococcal serum must be tried in hospital. He approved of the establishment of a standardizing laboratory. This arrangement had worked very well in America. When the products did not conform to the requirements, the licences were

either suspended or revoked. He claimed that the bacteriological tests for potency of anti-diphtheritic serum gave more accurate information than the clinical results as usually collected. In regard to the restrictions in the importation of sera and vaccines, he expressed the opinion that Australia had not suffered at all, since the products offered by the Serum Laboratories were of as great potency as the imported products.

He was interested to hear that pneumonia had been mild in Sydney during the past winter. In Melbourne it had been fairly serious. The typing of pneumococci by the isolation of the individual strains was not a slow process and was suited for treatment purposes. Information concerning the type of the organism could be obtained within a few hours with a reasonable degree of certainty by means of the intraperitoneal test in mice.

In regard to the question of delayed resolution, Dr. Penfold pointed out that it had been demonstrated that the simultaneous intra-tracheal injection of pneumococci and of normal dog serum in laboratory animals gave rise to pneumonia with delayed resolution. This was said to be due to the anti-tryptic properties of the serum. In reference to dysentery, Dr. Penfold stated that he was convinced that dysenteric infections were frequently missed. He related the discovery of *Bacillus dysenteriae* in one of his own children who was suffering several years ago from an apparently mild intestinal affection. Had he not been a bacteriologist, the faeces would certainly not have been examined. It was very necessary to make a serious study of dysentery in Australia. He admitted that antitetanic serum had yielded disappointing results in treatment.

### Obituary.

JOSEPH LIEVESLEY  
BEESTON.

It is not often that a medical practitioner who has laboured strenuously in the interests of his patients and of the community for a period of 39 years, is able to attend to his work with apparently unimpaired energy almost to the moment of his death.

Joseph Lievesley Beeston was in Newcastle for the purpose of visiting a patient on March 8, 1921. The visit finished, he sought assistance in getting into his car, an indication that he realized that he was ill. Instead of driving to his home in New Lambton, he directed his way to Hamilton where his eldest son, Dr. W. R. Beeston, carried him into his house. An hour and a half later he was dead.

Joseph Lievesley Beeston was born on September 19, 1859. He was the son of John Lievesley Beeston, then District Inspector in the New South Wales Railway Department. He was educated at the Newcastle High School.

After leaving school he became apprenticed to Dr. Samuel T. Knaggs in Newcastle. At the end of his term he journeyed to Ireland and at Dublin obtained the diplomas of the King and Queen's College of Physicians and of the Royal College of Surgeons of Ireland in 1882. In the same year he returned to Australia and on November 16 his name was entered on the Medical Register of New South Wales. He started practice without further delay in Newcastle. His ability as a practitioner, his earnestness and his sympathetic bearing soon gained recognition and led to early success. He preferred surgical work to that of a physician. After a few years' practice he was elected a member of the honorary staff of the Newcastle Hospital, where opportunity offered itself for the development of his surgical skill. His colleagues at the Hospital soon detected that

he was not only a competent surgeon, a delightful companion and an original thinker, but that he was also a "willing horse" whom they could utilize for hard work. He was selected for the position of Honorary Secretary of the Medical Board of the Hospital and filled this post for many years. He loved the work in the Hospital and was one of the most energetic members on the Board.

While his patients and his professional work claimed his attention before all else, he found time to devote to other pursuits and possessed the wit to bring benefit and advantage to many important undertakings. He was one of the founders and the first President of the Newcastle Agricultural, Horticultural and Industrial Association. He loved flowers and all the beautiful things in nature and realized how sterile and barren life would be without embellishments. He was a keen politician and held the opinion that those who possessed the ability, were under an obligation to their country to endeavour to improve its government. In the year 1908 he was elected a member of the Legislative Council. His political opponents respected him and admired the astuteness of his

judgement and the value of his spoken and written opinion. He took a real interest in the Newcastle School of Arts and both as its President and as a member of its management he expended time, trouble and intelligence in the conduct of its affairs. He was a prominent Free Mason and attained high rank.

In the year 1891, Joseph Lievesley Beeston obtained a commission as Captain in the Australian Army Medical Corps. He accounted it a privilege as well as a duty for a man to give his best service to his country. In those days the Army Medical Corps was composed of a small band of patriots, remarkable for their enthusiasm and the earnestness of their determination to be ready for all emergencies. He was promoted to the rank of Major in 1903 and six years later he became a Lieutenant-Colonel. When





war broke out he was over 54 years of age. He had already received the Victorian Decoration for long service. Shortly after his fifty-fifth birthday he was appointed full Colonel and placed in command of the Fourth Field Ambulance. He landed in Gallipoli on April 25, 1915. The value of his services on the peninsula is known to all. After having given sterling work in the ambulance, he was appointed Acting Director of Medical Services with the Second Anzac Division. For his gallant and devoted service he was mentioned in the dispatches of General Ian Hamilton, Commander in Chief of the Mediterranean Force. Early in 1916, he was invalided to England, as a result of the strenuous work in Gallipoli. His Majesty the King decorated him as a Commander of the Most Distinguished Order of Saint Michael and Saint George. He returned to Australia later in 1916 and soon resumed practice. Unfortunately the war had left indelible marks on him, as it had done on many other brave, unselfish men. But while his health had been undermined and his powers of sustained endeavour diminished, his spirit, the will to do his duty, had remained unchanged. During the few years that remained he was the genial, delightful companion and friend of yore; his patients found him as sympathetic and helpful, as skilled and as confident as before. His love for flowers and dogs and men was part of his nature and was ineffaceable. Few men have gained more affection from their contemporaries and still fewer have earned it so well. He possessed the confidence of his medical brethren. In the year 1905-1906 he filled the coveted position of President of the New South Wales Branch of the British Medical Association. Neither before nor since has any practitioner living outside the metropolitan area of Sydney been chosen for this office. He was regarded as the backbone, the iron support of the Central Northern Medical Association.

The medical profession in New South Wales and indeed in the greater part of Australia mourn his loss with his widow, his aged mother, his daughter and his two sons, Dr. W. R. Beeston and Lieutenant-Commander S. L. Beeston, Royal Australian Navy.

#### THE ROYAL PRINCE ALFRED HOSPITAL.

The annual report of the Directors of the Royal Prince Alfred Hospital for the year ended June 30, 1920, has been published, together with a large amount of printed matter, in book form. We presume that the primary object of this publication is to increase the amount of money subscribed by the charitable public. If this surmise be correct, the appearance of many pages of tables of diseases and operations, the repeated advertisement of the names of honorary and resident medical officers and information of an analogous kind would seem to have no justification. On the other hand, if the publication is intended to be used as a record of the scientific work carried out within the institution, the data available will be found to be wholly inadequate. We would suggest that the annual reports of the great metropolitan hospitals of Australia and the appendices attached to these reports should be compiled in such a way that useful information may be offered to those who are concerned in the institutional treatment of disease. Useless tables containing a rough classification of diseases and the number of patients treated, cured, relieved, unrelieved or dead, might with advantage be replaced by statistical information drawn up for the purpose of recording the frequency of well-defined pathological lesions and the results of different methods of treatment.

#### General Statistics.

On the first day of the twelve months under review there were 464 patients under treatment. The number admitted during the year was 7,077. The number of patients discharged was 6,658, of those who died was 410 and of those who were still under treatment on June 30, 1920, was 472. The statement is made that the mortality after deducting 108 deaths which occurred within 24 hours of admission, was 4.005%. Apart from the absurdity of calculating a mortality rate affecting approximately 7,000 persons to the third place of decimals, the calculation is incorrect. The gross mortality was 5.6%. The mortality after reduction of

108 patients who died within 24 hours of admission, was 3.3%.

Of the 7,077 patients admitted during the year, 3,073 contributed towards their cost of maintenance, while 715 were admitted at the cost of the Department of Defence and the Department of Repatriation. The number of patients treated gratuitously was therefore 3,289. The total amount paid by the patients was £8,173, which represents an average of £2 13s. 2½d. per patient. The average length of stay of the total number of patients is given as 23.13 days. We may assume that the average length of stay of the paying patients was approximately the same or in other words, that the patients paid at the rate of nearly 2s. 3½d. per day. The military and repatriation authorities, on the other hand, paid £18 1s. 5½d. per patient, which would be equivalent to 15s. 8½d. a day, presuming that the average length of stay was the same for all classes. From the balance sheet we learn that the total cost of maintenance was £94,231. This represents maintenance costs at the rate of £13 6s. 5½d. per patient per year or 11s. 10d. per patient per day.

#### Operations.

A table is published which will probably impress the public. It reveals the increase in the number of operations and percentage of patients operated upon since the year 1883. In 1883, 147 operations were performed; of each 100 patients 13.75 were subjected to the surgeon's knife. The proportion sank to 11.5 in the following year, but from that time onwards it increased steadily until the years 1916 to 1918, when over three quarters of those admitted underwent operative treatment. We have on more occasions than one drawn attention to the unfortunate tendency in Australian hospitals to reserve a very large proportion of the beds for persons requiring operation. In the year under review 5,053 operations were performed and 67% of the patients admitted underwent operations. It is improbable that of all the serious ailments affecting members of the general community, only one third are best treated by medical means. Our hospitals should not be converted to surgical institutions. We may assume that the proportion of patients admitted to surgical wards would have been higher, had it not been that for two months the wards set aside for persons suffering from influenza were still crowded.

#### Special Departments.

The number of persons treated in the Out-patient and in the Casualty Departments was 33,461. The Board agreed to increase the number of patients under treatment at one time in the venereal diseases clinic to 450 at the urgent request of the Government. The Board pointed out, however, that until a new block was built, the increase must be regarded as a temporary measure. The number of patients admitted into the Hospital for the treatment of syphilis was 137 and for the treatment of gonorrhoea was 146. A special department called the Anti-tuberculosis Dispensary exists for the out-door treatment of consumptives. The new patients numbered 510. No less than 199 patients suffering from pulmonary tuberculosis were admitted to the wards of the Hospital. Arrangements are made for the transference of these patients to sanatoria or to their own homes as soon as their condition permit of their removal.

The Medical Gymnastic and Massage Department exists also for the treatment of out-patients. During the year 1,029 received treatment in this Department.

In the Social Service Department arrangements were made for the transference of 888 of the patients to convalescent homes and of 118 to other institutions.

A new operating department is to be opened and will be known as the Anderson Stuart Operating Department. There will be six operating theatres concentrated in one block.

The report contains reference to additional buildings and equipment including a new kitchen, a new recreation hall, a cold storage installation and additional accommodation for the nurses.

#### The Hospital as a Clinical School.

It is impossible owing to the lack of space to deal in detail with the report of the Medical Superintendent or with the tables of "statistics of diseases treated." Mention, however, should be made of the fact that the Medical Superintendent should not include in his statement of the results of treatment the patients who were still under treatment at

the end of the year. For example, he writes under the heading "lobar pneumonia" that 96 cases (he means patients) were admitted during the year and that 16 of these died. It appears that twelve of these patients were still under treatment on June 30, 1920, that 68 had been discharged and that 16 had died. The mortality was nearly 18% calculated by the recognized method of the Registrar-General.

The number of students serving as clinical clerks and dresser has increased since the publication of the last report. It was 300 during the twelve months under review. It is stated that the proportion of students attending at this hospital to those attending at the Sydney Hospital is as 4:3, so that the number at the Sydney Hospital would have been 225. It is held that the number of patients at the hospital is not large enough for teaching so many students. It is hoped that a third clinical school will soon be established in another of the metropolitan hospitals. We have expressed the opinion that it would be advantageous if all the larger hospitals were invited to enter into arrangement with the Medical School of the University to widen the field for clinical study and to render individual tuition more practicable.

The report contains a considerable amount of information, but little that can be put to scientific use. Exception must be taken to the statement published both on the cover of the book and in the text that 4,187 in-patients were cured during the year 1919-1920. A glance at the statistical tables shows, for example, that there were 289 patients whose treatment for malignant disease was completed during the year. Of these patients 50 died; while 239 were discharged. In the table it is claimed that 79 were discharged "cured." It requires but small knowledge to recognize that the prognosis of malignant disease of the lip, of the stomach, of the œsophagus, of the breast, of the uterus and of the intestines even when the operation is performed at a favourable period, is by no means good. Probably many of these unfortunate patients, who are entered as "discharged cured," have since died of their disease. It is unwise to make exaggerated claims of this kind.

#### THE PARKIN PRIZE.

The Royal College of Physicians of Edinburgh announces that a prize is offered for the best essay on certain subjects connected with medicine. This prize is known as the Parkin Prize and is established in accordance with the terms of a bequest made by the late Dr. John Parkin. The value of the prize is £100. Essays on "the effects of the volcanic action in the production of epidemic diseases in the animal and in the vegetable creation and in the production of hurricanes and abnormal atmospheric vicissitudes written in the English language" will be received by the Secretary of the Royal College of Physicians of Edinburgh, Dr. J. S. Fowler, not later than December 31, 1921. Each essay must bear a motto and be accompanied by a sealed envelope bearing the same motto on the outside and the author's name enclosed. The successful candidate must publish his essay at his own expense and present a printed copy of it to the College within three months of the adjudication of the prize.

The announcement has been made that Mr. G. H. Knibbs, C.M.G., the Commonwealth Statistician, has been appointed Director of the Institute of Science and Industry. The salary attaching to this position is £2,000 a year.

#### Correspondence.

##### PAPILLOEDEMA.

Sir: May I crave your indulgence and space in the *Journal* for some remarks on papilloedema, with special reference to "ocular plumbism"? This name for the cases I see appears to be less misleading than "lead enccephalopathy," although they are really cases of this last. To apply so high sounding a title to the early cases which exhibit

merely a recent paralytic squint and papilloedema, might make those on whom we rely for early provisional diagnoses, hesitate to disclose them.

Professor Mills's very thoughtful paper on papilloedema includes a very concise statement of my published views regarding ocular plumbism in children. It indicates "in a nutshell" what I have endeavoured to hand on from my observations. This is gratifying, because it has at times occurred to me that I cannot have succeeded in making myself quite clear. No doubt it is an easy task to make one's arguments clear to Professor Mills.

Your sympathetic leader<sup>1</sup> on papilloedema following his paper should encourage those who do not accustom themselves to recognize early papilloedema, to do so and thereby prevent the very serious consequences of its non-recognition.

You very rightly find fault with the confusion of papilloedema, the modern name for "choked disc," with optic neuritis. Professor Mills, probably without really meaning it, says that papilloedema is the modern name for optic neuritis, which really is not the case. In my remarks at the discussion I was careful to draw this distinction, which I hope to amplify later in this note. Professor Mills's explanation of how the choroid gland is stimulated to extra secretion is interesting. That lead poisoning in children is apt to induce an over-secretion of cerebro-spinal fluid my cases prove; that this over-secretion is due to increased activity of the choroid gland seems likely. Whether lead in circulation causes this over-secretion indirectly by means of a brain extract or by direct stimulation, cannot be very easily decided. The statement in your leader that lead does not excite the choroid gland to secrete, but induces the fundus changes through the intervention of the kidneys, if accepted, could not explain the fact that the plumbic cases we see in children do not exhibit albuminuria or other evidences of kidney disease and that the fundus changes are those of papilloedema and not of optic neuritis. The fundus changes accompanying chronic nephritis and even those observed in the albuminuric retinitis of pregnancy do not include papilloedema.

Renal cases are essentially a neuro-retinitis. The most marked condition being patches of retinitic exudation accompanied by a varying amount of optic neuritis without appreciable swelling of the discs.

I can speak from considerable experience of cases of albuminuric retinitis and from very considerable experience of papilloedema due to lead in young children. I have little or no experience of fundus changes in the plumbism of adults and cannot therefore speak with any authority regarding them. It is difficult to believe that they differ materially.

Professor Mills is right in stating that the fundus appearances of ocular plumbism are identical with those of cerebral tumour. He may be right in considering that lead acts indirectly on the choroid gland, as he thinks tumour growth does. In the case of plumbism, however, we have lead circulating in the blood, as is proved by the fact that it is to be found in the urine and that it often leads to a blue line of sulphide of lead in the gums. For some years now it has been a routine practice at the Brisbane Hospital for Sick Children to have the blood of all possible lead cases examined by our pathologist for basophilic. It is invariably found in both the general and the ocular cases, except occasionally in very early ones.

Whether we regard the basophilic bodies as arrests in the development of non-nucleated red cells from nucleated ones, or as a degeneration of the young red cells, they indicate that the presence of lead in the circulating blood profoundly influences the red cells of the blood at the time when they are in a transition state between nucleated and fully developed cells and while they are still in the blood-forming organs. To me the bodies appear to be fragments of breaking down nuclei. The fact that de-ionization results in a deposit of lead on the negative plate and that it is able to get rid of pronounced blue lines on the gums is further evidence of the presence and distribution of lead.

Yours, etc.,

J. LOCKHART GIBSON.

March 3, 1921.

It is with regret that we have to announce the death of

<sup>1</sup> February 26, 1921.

Dr. William Stuart Hawthorne, of Murrayville, Victoria, which occurred on March 13, 1921.

#### INCOME TAX IN THE UNITED KINGDOM.

We have received the following letter from Mr. Wilfred T. Fry (Fry and Morrison), Walter House, 418-422 strand, London W.C. 2, dated February 7, 1921:

By a concession granted under the *Finance Act, 1920*, all British subjects resident in the colonies or abroad are granted the right of reclaiming British income tax as though they were resident in this country.

The result of this concession is that any of your readers who derive taxed income, such as dividends, rents, annuities, etc., from the United Kingdom can now recover the whole or part the tax deducted. If dividends or interest are received "free of tax" a claim for refund can still be made.

I have for many years interested myself in this subject and have constantly advocated that this concession should be made. I shall be pleased to advise, without charge, any of your readers who care to write to me as to whether they have a claim for repayment and if so, how it should be prepared.

#### Books Received.

THE DIARY OF AN AUSTRALIAN SOLDIER (Captain K. J. Barrett); 1921. Melbourne and Sydney: The Lothian Book Publishing Co., Pty., Ltd.; Demy 8vo., pp. 135.

PRINCIPLES OF BIO-CHEMISTRY: For Students of Medicine, Agriculture and Related Sciences, by T. Brailsford Robertson, Ph.D., D.Sc.; 1920. Philadelphia and New York: Lea and Febiger; Royal 8vo., pp. 633, with 49 engravings.

MANUAL OF MEDICAL JURISPRUDENCE AND TOXICOLOGY, by W. G. Aitchison Robertson, M.D., D.Sc., F.R.C.P.E., F.R.S.E.; Fourth Edition. London: A. & C. Black, Ltd.; Crown 8vo., pp. 414, with 27 illustrations. Price, 12s. 6d. net.

MANUAL OF PUBLIC HEALTH, by W. G. Aitchison Robertson, M.D., D.Sc., F.R.C.P.E., F.R.S.E.; Fourth Edition. London: A. & C. Black, Ltd.; Crown 8vo., pp. 414, with 25 illustrations. Price, 10s. 6d. net; 11s. by post.

#### Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, locum tenentes sought, etc., see "Advertiser," page xxiii.

Isisford District Hospital, Queensland: Medical Officer.  
Imperial Bacteriological (Veterinary) Laboratory, Muktesar, India: Director and First Bacteriologist, second Bacteriologist, Pathologist.

#### Medical Appointments.

##### IMPORTANT NOTICE.

Medical practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, 429 Strand, London, W.C.

Branch.	APPOINTMENTS.
<b>NEW SOUTH WALES.</b> (Hon. Sec., 30-34 Elizabeth Street, Sydney.)	Australian Natives' Association. Ashfield and District Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham Dispensary. Manchester Unity Oddfellows' Medical Institute, Elizabeth Street, Sydney. Marrickville United Friendly Societies' Dispensary. North Sydney United Friendly Societies. People's Prudential Benefit Society. Phoenix Mutual Provident Society.

Branch.	APPOINTMENTS.
<b>VICTORIA.</b> (Hon. Sec., Medical Society Hall, East Melbourne.)	All Institutes or Medical Dispensaries. Manchester Unity Independent Order of Oddfellows. Ancient Order of Foresters. Hibernian Australian Catholic Benefit Society. Grand United Order of Free Gardeners. Sons of Temperance. Order of St. Andrew. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association.
<b>QUEENSLAND.</b> (Hon. Sec., B.M.A. Building, Adelaide Street, Brisbane.)	Australian Natives' Association. Brisbane United Friendly Society Institute. Stannary Hills Hospital.
<b>SOUTH AUSTRALIA.</b> (Hon. Sec., 3 North Terrace, Adelaide.)	Contract Practice Appointments at Renmark. Contract Practice Appointments in South Australia.
<b>WESTERN AUSTRALIA.</b> (Hon. Sec., 6 Bank of New South Wales Chambers, St. George's Terrace, Perth.)	All Contract Practice Appointments in Western Australia.
<b>NEW ZEALAND: WELLINGTON DIVISION.</b> (Hon. Sec., Wellington.)	Friendly Society Lodges, Wellington, New Zealand.

#### Diary for the Month.

Mar. 30.—Vic. Branch, B.M.A., Council.  
Mar. 31.—S. Aust. Branch, B.M.A..  
Apr. 1.—Q. Branch, B.M.A..  
Apr. 6.—Vic. Branch, B.M.A..  
Apr. 8.—N.S.W. Branch, B.M.A., Clinical.  
Apr. 8.—Q. Branch, B.M.A., Council.  
Apr. 8.—S. Aust. Branch, B.M.A., Council.  
Apr. 12.—Tas. Branch, B.M.A..  
Apr. 12.—N.S.W. Branch, B.M.A., Ethics Committee.  
Apr. 14.—Vic. Branch, B.M.A., Council.  
Apr. 15.—North-Eastern Med. Assoc. (N.S.W.), Annual.  
Apr. 19.—N.S.W. Branch, B.M.A., Executive and Finance Committee.  
Apr. 20.—W. Aust. Branch, B.M.A..  
Apr. 22.—Q. Branch, B.M.A., Council.  
Apr. 22.—Western Med. Assoc. (N.S.W.).

#### EDITORIAL NOTICES.

Manuscripts forwarded to the office of this journal cannot under any circumstances be returned.

Original articles forwarded for publication are understood to be offered to *The Medical Journal of Australia* alone, unless the contrary be stated. All communications should be addressed to "The Editor," *The Medical Journal of Australia*, B.M.A. Building, 30-34 Elizabeth Street, Sydney. (Telephone: B. 4635.)